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## Chemo and enantioselective addition of grignard reagents to ketones and enolizable ketimines

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# **Chemo and Enantioselective Addition of Grignard Reagents to Ketones and Enolizable Ketimines**

**Pablo Ortiz**

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# **Chemo and Enantioselective Addition of Grignard Reagents to Ketones and Enolizable Ketimines**

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to obtain the degree of PhD at the  
University of Groningen  
on the authority of the  
Rector Magnificus Prof. E. Sterken  
and in accordance with  
the decision by the College of Deans.

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## List of Abbreviations

ACA: Asymmetric conjugate addition

Bus: *tert*-butyl sulphonyl

Brij10: Polyoxyethylene (10) oleyl ether

Ch: Choline

*ee*: enantiomeric excess

DCE: dichloroethane

DCM: dichloromethane

DES: Deep eutectic solvent

DMF: Dimethylformamide

DOSY: Diffusion-ordered spectroscopy

DPP: Diphenylphosphinyl

ECC: External calibration curve

EDG: Electron-donating group

EWG: Electron-withdrawing group

EXSY: Exchange spectroscopy

Gly: Glycine

HMPA: Hexamethylphosphoramide

LA: Lewis acid

LG: Leaving group

*m*-CPBA: *meta*-Chloroperbenzoic acid

MPV: Meerwein-Ponndorf-Verley

MW: Molecular weight

MWI: Microwave irradiation

NHC: N-heterocyclic carbene

NOE: Nuclear Overhauser effect

NOESY: Nuclear Overhauser effect spectroscopy

PG: Protecting group

TBAF: Tetrabutylammonium fluoride

Tf: Trifluoromethanesulfonic

THF: Tetrahydrofuran

TMEDA: Tetramethylethylenediamine

TMS: Tetramethylsilane

TPhN: 1,2,3,4-tetraphenylnaphthalene

TPGS-750-M: Polyoxyethanyl- $\alpha$ -tocopheryl succinate

Ts: Tosyl, *p*-toluensulfonyl

VCD : Vibrational circular dichroism

W: Watts



Lord Polonius: What do you read, my lord?  
Hamlet: Words, words, words.  
Lord Polonius: What is the matter, my lord?  
Hamlet: Between who?  
Lord Polonius: I mean, the matter that you read, my lord.

William Shakespeare, *Hamlet*

This chapter introduces the importance and methods of synthesis of chiral  $\alpha$ -tertiary alcohols and amines. Our approach to synthesize them by asymmetric addition of Grignard reagents to ketones and ketimines is based on the discovery made by our group in 2012 of a Cu(I)-chiral diphosphine ligand catalyst that allowed the catalytic enantioselective 1,2-addition of alkyl Grignard reagents to enones and ketones.